REMARKS

Claims 88-98 are pending. Claim 88 has been amended. No new matter has been added by way of the present amendment. Moreover, the nature of the amendment does not require any additional search on the part of the Office. As such, entry of the amended claims and considerations of the remarks provided below is respectfully requested.

Withdrawn objections and rejections

Applicants gratefully acknowledge the Office's steps to withdraw the objection to the Oath or Declaration, the objection to claim 4, and the withdrawal of all previous rejections.

Alterations to the Specification

Applicants acknowledge the comments of the Office regarding the specification and the allegedly embedded hyperlinks and the like. Applicants submit that the amendments made to the specification change the nature of the text objected to by the Office into non-browser-executable code. Nevertheless, solely to advance prosecution of the present case, Applicants have further amended the specification to remove the objected to text. Thus, this issue has been overcome.

Examples 13, 36 and 37

The Office has alleged that the titles of Examples 13, 36 and 37 contain typographical errors. A heading in Example 13 was found to contain a typographical error and was corrected. Errors in capitalization were noted in Examples 36 and 37, which were corrected. The Office is invited to specify additional errors, if any, that exist in the cited examples so that appropriate correction can be made.

Patentable Subject Matter

Claims 88-98 were rejected under 35 U.S.C. § 101, as allegedly reciting non-statutory subject matter. Specifically, the Office has alleged that claim 88 does not distinguish an antibody that binds SEQ ID NO: 728 as it exists in nature. Although Applicants respectfully disagree with the Office regarding the reasons for the present rejection, solely to advance the prosecution of the present case, claim 88 has been amended to recite an isolated antibody or fragment thereof. This amendment removes the reasons for the present rejection.

Utility

The Office rejected the pending claims as allegedly lacking utility. To be useful, a claimed invention must be supported by a credible, specific, and substantially asserted utility or a well established utility. As shown in the specification, mRNA encoding the claimed protein was expressed in cancer tissues and was only expressed in normal testis tissue (see Example 4). Because of this differential expression pattern, Applicants submit that antibodies directed to a protein having at least 90% homology to SEQ ID NO: 728 have utility as diagnostic and treatment agents for cancer.

The Pending Claims are Novel

Claims 88-95 and 97-98 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Tang, *et al.*, WO 01/53312. To be anticipatory a reference must teach each and every limitation of the claimed invention.

Here, WO 01/53312 was published 26 July 2001, which is after the filing date of the present application. The WO 01/53312 reference does claim priority to applications filed before the earliest priority of claimed by the present application, specifically, August 28, 2000. The claim for priority in the relevant time period consists of the following applications: 09/488,725 (21 JAN 2000), 09/552,317 (25 APR 2000), 09/598,042 (9 JULY 2000), 09/620,312 (19 JULY 2000) and 09/653,450 (3 AUG 2000). Application No. 09/620,312, filed July 19, 2000, issued as U.S. Patent

No. 6569662 and was a continuation-in-part application of U.S. Application No. 09/552,317, filed Apr. 25, 2000, which in turn is a continuation-in-part application of U.S. application Ser. No. 09/488,725, filed Jan. 21, 2000. These cases are underlined.

The sequence listing for Application No. 09/620,312 (now U.S. Patent No. 6,569,662) is available on-line from the U.S. Patent and Trademark Office. The claimed sequence is not disclosed in the issued patent. Thus, Applicants conclude that the relevant sequence was not disclosed in this line of patent applications which includes 09/488,725 and 09/552,317. The Office is in a better position than Applicants to confirm or deny this assertion.

A copy of the specification for Application No. 09/653,450 was ordered and inspected. The sequence listing of the 09/653,450 application, filed August 3, 2000 discloses the presently claimed amino acid sequence as SEQ ID NO: 174. Applicants' priority date is August 28, 2000, thus this reference was filed twenty-five days before Applicants' earliest priority date.

Applicants submit with this response a declaration under 37 CFR § 1.131 which avers that Applicants were in possession of the claimed sequence before the filing date of the 09/598,042 application. As such, this reference is removed as prior art against the pending claims. Therefore, the present rejection should be withdrawn.

The Pending Claims are Not Obvious

Claims 88-95 and 97-98 were rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Williams *et al.* (Mol Microbiol. 1998 Jan;27(1):171-86) in view of Campbell, A. (Monoclonal Antibody Technology), Queen, *et al.* (U.S. Patent No. 5,530,101) and Reiter, *et al.* (U.S. Patent No. 6,261,791). To articulate a *prima facie* case of obviousness, the Office must articulate, *inter alia,* one or more references that teach or suggest the claimed invention and a motivation to combine or modify those references to achieve the claimed invention. Here, the Office has failed to articulate a motivation to combine or modify the cited references to achieve the claimed invention.

The Williams *et al.* reference used a yeast two-hybrid system to identify human epithelial cell proteins that interact with *Neisseria gonorrhoeae* opacity-associated (Opa) proteins. The Williams *et al.* reference identified an Opa interaction protein sequence (OIP5) that was identical to the claimed sequence. Williams *et al.* did not make antibodies against this protein. To remedy this deficiency, the Office cited Campbell *et al.*, Queen *et al.* and Reiter *et al.* to supply the missing teachings for the production of antibodies generally, for the production of monoclonal antibodies, for the production of antibody fragments and for teachings regarding the production of labeled antibodies and fragments thereof. None of these references provides the requisite motivation to combine the cited teachings to achieve the claimed invention.

The Office suggests in the Action that it is "customary" for skilled artisans to make monoclonal antibodies against genes that have been cloned. Apparently the Office intends for this observation to serve as the motivation to combine the cited references to achieve the claimed invention. (Office Action, page 20, first full paragraph.) The observation provided by the Office amounts solely to an "obvious to try" rationale, which, under U.S. law is not sufficient to support a prima facie case of obviousness. Accordingly, in light of this deficiency in the Office's *prima facie* case of obviousness, Applicants request that the present rejection be withdrawn.

The Office goes on in the Action to argue that the Board of Patent Appeals and Interferences has established a *per se* rule that once an protein has been isolated, that the manufacture of monoclonal antibodies that recognize the protein are *prima facie* obvious. *Id.* The Office cites *Ex parte Ehrlich* and *Ex parte Sugimoto* to support this position. Applicants respectfully disagree with the Office's characterization of the law.

It is unclear to Applicants why *Ex parte Sugimoto* (14 USPQ2d 1312 (BPAI 1990)) was cited. This case does not concern the production of monoclonal antibodies nor does it opine on the alleged obviousness of a monoclonal antibody raised against a known protein.

Applicants do agree that *Ex parte Ehrlich* (3 USPQ2d 1011 (BPAI 1985)) is relevant to the present discussion. In this case, antibodies against a known antigen were considered obvious. What

the Office does not comment on is the distinction between a known antigen and a known protein. The board in *Ehrlich* found that the present of interest in that case was a "known antigen". (*Id.* at 1015.) The board seemed moved by the power of the method of Kohler and Milstein to produce monoclonal antibodies to known antigens. This case, however, is completely silent regarding the distinction between a known antigen and merely a known amino acid sequence. Those of ordinary skill in the immunological arts readily recognize that just because one knows the amino acid sequence of a protein does not immediately imply that one knows if that amino acid sequence is antigenic, *e.g.*, is capable of eliciting antibody production from a host.

The board in *Ex parte Ehrlich* discusses the case of *Ex parte Old* (229 USPQ 196 (BPAI 1985)), which is relevant here. In *Ex parte Old*, the examiner had rejected monoclonal antibody claims based on the existence of polyclonal antibodies in the art and the teachings of Kohler and Milstein. (*Id.* at 199.) The board reversed the examiner, stating:

> We cannot subscribe to this rationale. Although the technique underlying hybridoma technology is well recognized . . . . [h]ybridoma technology is an empirical art in which the routineer is unable to foresee what particular antibodies will be produced and which specific surface antigens will be recognized by them. Only by actually carrying out the requisite steps can the nature of the monoclonal antibodies be determined and ascertained . . . .
>
> It is here also appropriate to observe . . . that if the art of monoclonal antibodies to cancer antigens were routine and predictable then the Kohler-Milstein discovery would make obvious all monoclonal antibodies to cancer antigens and the field of cancer immunology would have routinely produced cancer cures. Such, manifestly, has not happened. Rather it is the purpose and aim of the patent system to encourage and foster advances aimed towards attaining this objective and such can only be accomplished by the grant of patent protection to inventions of the nature as here at issue which concededly are novel and palpably also unobvious. (*Id.* at 200.)

In light of the failure of the Office to articulate a *prima facie* case of obviousness, based either on the cited reference or on the existence of some *per se* rule of antibody obviousness, Applicants respectfully submit that the subject matter of the pending claims is both novel and unobvious. As such, the present rejection of the claims should be withdrawn.

The Office further rejected claims 88-98 under 35 U.S.C. § 103 as allegedly being unpatentable over Tang *et al.* (WO 01/53312) in view of Reiter, *et al.* (U.S. Patent No. 6,261,791). For the reasons discussed above, the Tang *et al.* reference is not available as prior art against the present case. Accordingly, the Office has failed to articulate a *prima facie* case of obviousness based upon these cited references. As such, this rejection should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582002800.

Respectfully submitted,

Dated: March 17, 2005 By: _____

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